REMARKS

Claims 1-10 have been presented for examination and rejection by the Examiner. By this amendment the Applicants amended claims **1-7.**

Reexamination and reconsideration of the Application as amended is requested.

The Applicants respectfully traverse the Examiner's rejection for the following reasons and make clarifications to the claimed invention.

35 U.S.C. §112

Claims **1-10** were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention. More specifically, the Examiner cited terms "whereby" and "specified amount " of claim 1, "so as" of claims 3-4 and "specified temperature level " of claims 5 and 6. The Applicants amended claims 1, 3, 4, 5 and 6 to recite every element of the claimed invention in a clear, positive and definite way.

35 U.S.C. §103

Claims 1-10 were rejected under 35 U.S.C. §103 (a) as being unpatentable over Marek (US patent 6,437,570) in view of Bartuska (US patent 5,146,166).

Marek is cited as a primary reference. The Examiner states that both independent claims 1 and 7 , similar to Marek teach " an NMR probe including a flow cell and inlet tubing connected to said flow cell, providing a heater comprising a twisted-pair wire to thereby generate heat…". The only difference that the Examiner identified between the claimed invention and Marek's teaching is the absence in Marek's patent of the requirement of the pre-heating of the liquid before reaching it the flow cell. The Applicants respectfully disagree with the Examiner's rejection for the following reasons.

Marek invention relates to a NMR probe head, which is connected to a room temperature pipe having a sample tube with a sample, disposed therein, wherein the NMR probe head is working in a specific cryogenic environment. Marek tries to "prevent dissipation of heat from the measuring sample and thus uneven cooling without significantly impairing the received NMR signals" (see col.2. lines 16-18). Further Marek states that that the following heating means may be utilize to achieve the objectives:

"through heating with electric current but also heating through radiation or thermal conduction in the region about the sample tube.

A particularly preferred embodiment...comprises a layer radially surrounding the sample tube in the axial region...Absorption of thermal radiation in the layer permits temperature control of the sample tube in the corresponding axial region."

In other words, Marek describes a method of compensating for radiative heat loss into a cryogenic environment specifically in the "sweet" spot or the analysis region of the radio frequency coil. The objective of his invention is not to heat the actual liquid sample, but rather provide an active insulator from the cryogenic environment. For this purpose Marek suggests to use tempering means 11 with a heatable element that surrounds the sample tube 6. He is suggesting a twisted coil as one possible means of heating, or in more precise definition, "defrosting" the insert tube. The choice of the twisted coils as disclosed in the patent is conventional. It is well known that when current is passed though a coil, the coil develops a magnetic field of certain strength and polarity that may be canceled by inducing the equal magnetic field having opposite direction that is provided by the second coil. However, in spite of the fact that twisted coils circuitry of Marek and the present invention are similar due to basic physics laws requirement of compensating for the induced magnetic fields, they are utilized for essentially different purposes.

Marek's invention is aimed to decrease temperature gradients along the sample tube. To better appreciate the difference between the subject invention and Marek's teaching, the Applicants suggested very simple analogy from unrelated art of the defrosting mechanism in the car. The wires in the window increase the temperature of the window for slightly warming it above the ambient dew point to minimize condensation thereon, but not heat the passenger compartment.

According to the subject invention the liquid sample is directly heated by heat generated from the resistance of the current passing through deliberately selected not-magnetic wire. The subject invention provides efficient way to heat a long tube with a liquid sample passing therethrough. The long tube is tightly and helically wrapped in a resistive wire as shown in Fig. 2 that heats directly the liquid sample evenly along the length of the tube before entering the "sweet spot" of the NMR probe.

The twisted –pair wire is applied to the whole length of the inlet tubing being extremely close to the magnetic field and not disturbing it. The selection of the wire is made according to these special conditions. As it seen in Fig. 2 the long wires, literally folds in half is twisted like a rope and then coil this twisted pair around the tube. This double twist allows for better magnetic self-

compensation and minimizes the generation of superfluous radio frequency fields, which could potentially increase the noise level in the NMR data.

Therefore the subject invention has different then Marek's invention objectives and technical implementation corresponding to these objectives.

The Examiner combines the Marek teaching with teaching of the secondary reference, the US patent issued to Bartuska. Batruska teaches a sample management system that uses a guide tube to introduce a sample contained in a small sealed tube to the spectrometer. When the sample has arrived to the "analysis" region of probe NMR data is acquired and the sample exits the magnet via a trap door at the base of the "analysis" region through the bottom end of the magnet. Among the objectives of the invention Batruska mentions that his method and design "allow the NMR samples to be pre-heated or pre-cooled to a required temperature before entering the analysis area of the spectrometer". In the description of the preferred embodiment section of the specification he explains what kind of pre-heating is utilized in his invention as follows:

> " The introduction of the thermostatting device (not shown) into first storage rack (4) may further enhance the speed of analysis. Typically, samples are inserted by an automatic sample changer and a certain amount of time is required for the sample to reach a required analysis temperature. In this embodiment each sample is brought to the proper analysis temperature while positioned in first storage rack (4) by the thermostatting device...

For some applications a thermostatting device may also be used in second storage rack (5)" (col. 9, lines 66-68-col.10, lines 1-10).

Therefore, Batruska suggests that the independently sealed sample tube may be heated or cooled while sitting in the sample rack-awaiting introduction to the NMR spectrometer. This type of heating or cooling devices is well known in the art and commercially available. However they are not generally applied to the situation where a sample is introduced to the " analysis region" or active region of the flow cell via a fluidic pathway as requested by the present invention.

According to the claimed invention, the sample is introduced via a thin stream of liquid passing though a tube that is connected to the flow cell. Batruska does not teach directly or indirectly how to heat or cool the sample in the "transfer" region. It was known in the art at the time when the subject invention was made that there are commercially available devices that may heat the LC or robotics system where the sample rests before introduction to a flow system.

None of the prior art reference teaches how to span the distance from the base of the NMR probe to the active region of the flow cell while maintaining the sample temperature as it enters the base of the probe or actually heating it to the desired temperature as it traverses the distance from the base of the probe to the active region of the flow cell. The subject invention addresses this problem and suggests the solution. The active region of the flow cell has its own temperature regulation. Since the narrow steam of liquid is passing through a tube, the tubing material itself removes heat from the sample. Therefore, due to the fact that the inlet tubing is actively heated by means not altering the magnetic field or increasing noise in the data, the sample liquid expeditiously reaches the desired experimental analysis temperature (temperature at which the active region of the flow cell is maintained). The experimental data, for example, presented in the detailed description of the invention supports this statement. "Fig. 3 shows the spectra of temperature sensitive NMR signals collected immediately after 1ml of fluid was injected into the flow probe without preheating. The frequency of the signal changes as the temperature of the sample is equilibrating from 22°C to 48°C. The liquid in the flow cell is considered equilibrated when the frequency of the signal becomes stable. The time to reach equilibrium in this experiment was 95 seconds." (page 3, lines 13-17). This is a significant time-saving if one wishes to run thousands of samples at this particular temperature.

Applicants respectfully submits that Marek and Batruska references taken separately or in combination do not provide a suggestion or motivation for modifying their teaching to arrive at the subject matter of the instant claims.

In view of the foregoing amendments and remarks it is believed that the subject application is now in condition for allowance. Allowance of the claims pending in the application at an early date is respectfully solicited.

Respectfully submitted,

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